

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization  
International Bureau(43) International Publication Date  
7 June 2001 (07.06.2001)

PCT

(10) International Publication Number  
**WO 01/39615 A1**(51) International Patent Classification<sup>7</sup>: A23L 1/30, 2/38, 2/52, 1/09(74) Agents: JAMES, Anthony, Christopher, W., P. et al.;  
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(21) International Application Number: PCT/GB00/04608

(22) International Filing Date: 1 December 2000 (01.12.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
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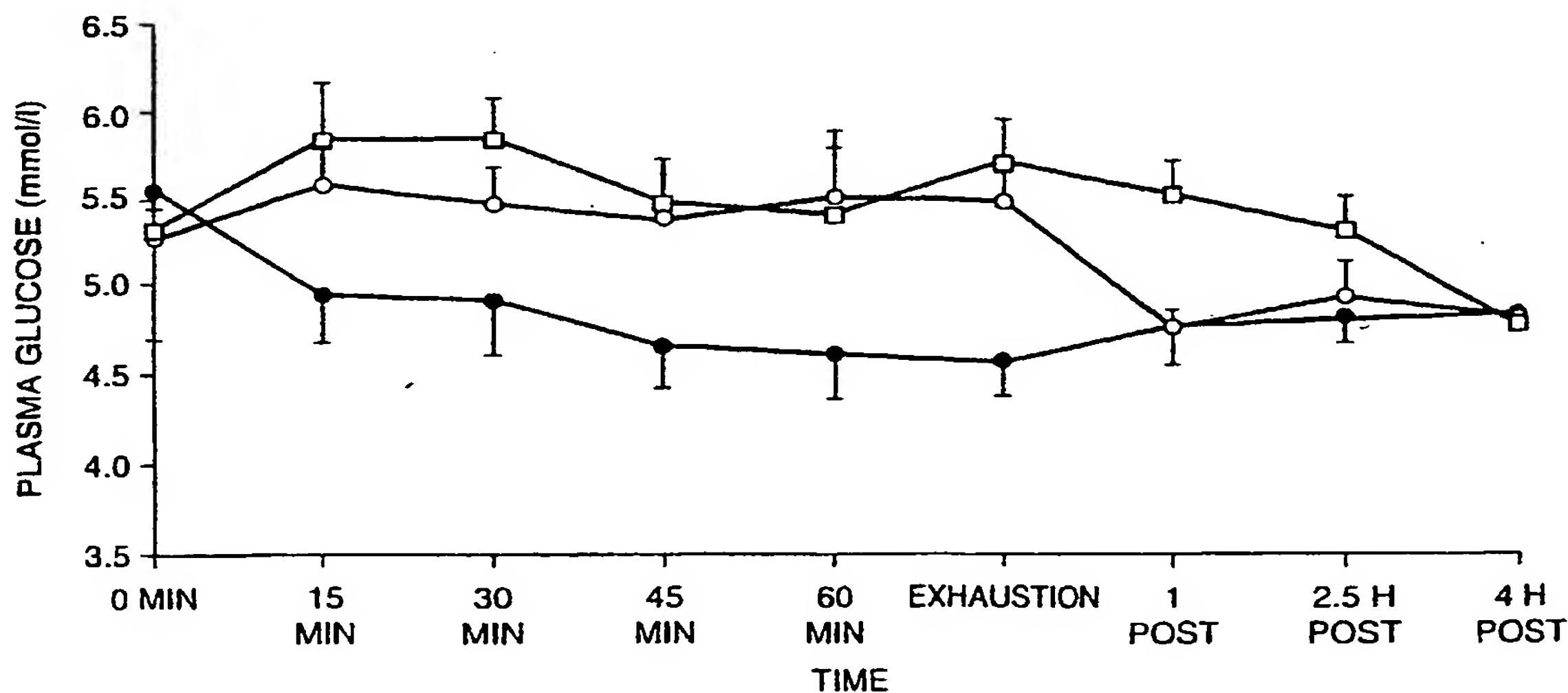
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- With international search report.
- Before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments.

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: USE OF SUGAR COMPOSITIONS



(57) Abstract: The invention provides the use of trehalose for the preparation of a nutritional composition for oral administration to a subject during or shortly before physical exercise to maintain the blood glucose level of the subject for a sustained period during and after said exercise. Preferably, the nutritional composition is sports drink.

WO 01/39615 A1

## USE OF SUGAR COMPOSITIONS

The present invention relates to the use of trehalose for the preparation of nutritional compositions for consumption during or shortly before physical exercise.

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It is now well established that the consumption of carbohydrate containing beverages is beneficial for endurance exercise performance. It has become a common practice in many sports for the participants to ingest sports drinks during both competition and training, for example in cycling, triathlon, marathon, football  
10 or rugby. It is also known for participants in recreational pursuits such as walking and disco dancing to consume carbohydrate containing beverages to improve endurance performance. The beverages are also consumed to improve mental-alertness during such activities.

15 Both the provision of fluid to replace sweat losses and the provision of an energy substrate, usually in the form of glucose and/or glucose polymers, are important considerations in the formulation of sports drinks. Fatigue during prolonged exercise is associated with both dehydration and depletion of endogenous carbohydrate reserves and low blood glucose concentration. Low  
20 blood glucose levels also impair mental concentration and motor skill.

Most drinks for use during exercise are isotonic. That is to say, they have a osmolality close to that of blood plasma, which is about 290 mmol/kg. Isotonic drinks are rapidly emptied from the stomach and absorbed in the intestine.  
25 Increasing the osmolality of the drinks by adding more glucose slows the rate of gastric emptying and initially draws fluid from the circulation into the gut, causing an undesirable dehydrating effect. Hence, most sports drinks contain glucose at a concentration of 4-6% w/v, together with a small amount of sodium (10-60 mmol/l, usually as sodium citrate) which optimises the rate of glucose and water  
30 absorption. Glucose is cotransported with sodium from the gut lumen into the gut epithelial cells, and water follows by osmosis. The addition of sodium at concentrations of 40-80 mmol/l aids retention of fluid in the body, and a

concentration close to 60 mmol/l has been recommended for drinks designed to promote post-exercise recovery.

Trehalose ( $\alpha$ -D-glucopyranosyl- $\alpha$ -D-glycopyranoside) is a naturally occurring non-reducing disaccharide found in fungi, certain yeasts, certain drought resistant plants and in the blood of insects. However, it has hitherto contributed an insignificant part of most human diets.

G. G. Birch in Process Biochemistry, July 1970, page 9, briefly reviews the role of trehalose in nature. The author notes that trehalose is quite sweet tasting, and if it were to be absorbed slowly or not at all by the body without any ill effect could produce a useful non-fattening dietetic or diabetic sugar.

It has subsequently been established that trehalose is, in fact, readily absorbed by the body. The mechanism for absorption is thought to be that trehalase enzyme in the microvilli of the small intestine breaks the trehalose down into its constituent glucose monomers, which are then absorbed through the intestinal wall.

WO96/08979 describes isotonic or hypotonic sports beverages containing trehalose. The sports beverages containing trehalose are said to be useful for providing rehydration and nutrition during athletic exercise. The use of trehalose rather than glucose is said to be desirable because of the lower osmotic pressure at a given weight concentration of trehalose (a disaccharide) compared to glucose (a monosaccharide). There is no suggestion that trehalose would be superior to glucose for sustained maintenance of blood glucose levels after prolonged exercise.

EP-A-0619951 describes energy supplements containing trehalose. Data are presented showing that relatively small orally administered doses of trehalose (apparently less than 0.01 g/kg of body weight) boost blood glucose levels. It was also found that the trehalose gives a slightly smaller, but still substantial, insulin response than the equivalent amount of glucose. There is no mention of

administration of compositions containing trehalose during or shortly before vigorous exercise to maintain blood glucose levels following said exercise. On the contrary, both this reference and WO96/08979 indicate that the main usefulness of trehalose in nutrition is to provide a quick boost to blood glucose levels.

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JP-A-9173017 describes edible compositions containing trehalose that are said to improve strength and stamina during exercise. There is no disclosure of prolonged exercise, nor is there any suggestion of improved recovery after exercise.

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It has now been found by the present inventors that administration of compositions containing trehalose during and/or shortly before physical exercise provides an improvement in exercise endurance time that is not significantly better than that achieved with glucose. However, the trehalose does not only provides a rapid boost to blood glucose levels; it also sustains the blood glucose level of the subject at near-normal levels for at least one hour following the exercise. The trehalose thereby promotes post-exercise recovery, particularly following prolonged exercise for 20 minutes or more. The trehalose reduces physical and mental impairment (fatigue) following such exercise.

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The long-term response to orally administered trehalose is quite different from the response to orally administered glucose, where a hypoglycaemic dip is observed following vigorous exercise that can give rise to feelings of increased exhaustion and reduced alertness of the subject.

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Accordingly, the present invention provides the use of trehalose for the preparation of a nutritional composition for oral administration to a subject during and/or shortly before prolonged physical exercise to maintain the blood glucose level of the subject for a sustained period after said exercise.

30

In another aspect, the present invention provides the use of trehalose for the preparation of a nutritional composition for oral administration to a subject

during and/or shortly before prolonged physical exercise to reduce physical and mental impairment of the subject following said exercise.

In another aspect, the present invention provides the use of trehalose for the preparation of a nutritional composition for oral administration to a subject during and/or shortly before prolonged physical exercise to promote post-exercise recovery.

Preferably the nutritional composition is selected from the group consisting of chocolate confectionery, sugar confectionery, biscuits, fondants, jellies, jams, sauces, puddings, syrups, soft drinks, sweet or savoury snack foods, cakes and other baked goods, ice cream, energy and cereal bars, alcoholic beverages and combinations thereof. More preferably, the nutritional composition is a soft drink, and most preferably it is a sports drink.

15

Preferably, the nutritional composition is in a unit dosage format. That is to say it is in a form adapted for consumption by a single human subject at substantially one time, for example a confectionery bar, an energy or cereal bar, or a bottle or can containing 100-500ml of beverage. Preferably, the unit dosage form contains more than 12g of trehalose, more preferably more than 20g of trehalose. Preferably, the nutritional composition is packaged in the unit dosage format.

Preferably, the composition used in the present invention comprises at least 10% w/w of trehalose, preferably at least 20% w/w of trehalose, more preferably at least 30% w/w trehalose, and most preferably at least 40% or 50% by weight of trehalose, based on the dry weight of the composition.

Where the composition is a soft drink, it may be somewhat hypertonic, but it is preferably an isotonic or hypotonic solution. Preferably, the osmolarity of the soft drink is 400 mOsm or less, more preferably it is 300 mOsm or less, and most preferably it is 250 mOsm or less. The concentration of trehalose in the soft drink is preferably 2 to 25 wt.%, more preferably 5 to 15 wt.%.

Where the composition is a soft drink, the step of preparation may comprise diluting a solid or liquid concentrate with water or carbonated water.

5 Preferably, the soft drink also comprises at least one salt in an amount sufficient to enhance uptake of the water through the gastrointestinal tract. Preferably, the salt is selected from the group consisting of salts of sodium, potassium, magnesium and calcium. Preferably, the salt is present in an amount of 10-100mmol/l, more preferably 40 to 80 mmol/l.

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In addition to trehalose and salts, the compositions may contain other nutrients. Suitable nutrients include monosaccharides such as fructose, mannose, galactose and glucose, and disaccharides other than trehalose such as sucrose, maltose and lactose. Suitable nutrients further include vitamins, minerals, amino  
15 acids, peptides and proteins. Suitable vitamins include vitamin C, the B vitamins, pantothenic acid, thiamin, niacin, niacinamide, riboflavin and biotin. Suitable minerals include iron, zinc, chromium, calcium, copper and magnesium. Suitable amino acids include the 20 amino acids utilised by humans.

20 The compositions may further include appropriate amounts of colouring, artificial and natural flavours, sweeteners and preservatives. The compositions may further include one or more stimulants such as taurine and caffeine.

In accordance with the present invention, the step of oral administration  
25 preferably comprises administration of at least 0.1 g of trehalose per kg body weight of the person, preferably at least 0.3g/kg and more preferably at least 0.5 g/kg. Preferably, the step of oral administration comprises administration of a dose containing more than 12 g of trehalose to the human subject, preferably at least 20g and more preferably at least 25g.

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Preferably, the physical exercise is vigorous exercise, and more preferably the physical exercise is exercise substantially to exhaustion. Suitable forms of exercise include running, football, tennis, basketball, squash, housework, dancing

and the like. Preferably, the duration of the exercise is at least 20 minutes, more preferably 30 minutes or more.

The present invention is based on the surprising discovery that  
5 consumption of trehalose provides a sustained boost to blood glucose levels that lasts for considerably longer than the boost given by an equivalent molar quantity of glucose. In particular, consumption of trehalose seems to maintain the blood glucose level for an extended period even after exercise to exhaustion.

10 The term "maintain" used herein in relation to blood glucose levels signifies that the trehalose provides a blood glucose level that is higher in a statistically significant amount than is observed for a placebo containing an equivalent amount of water and no carbohydrate. Preferably, in the use according to the present invention, the blood glucose level is maintained at a level at least 0.25 mmol/l  
15 above the level for a carbohydrate-free placebo of equal liquid volume, and more preferably at least 0.40 mmol/l above that level.

Preferably, the blood glucose level is maintained for at least 90 minutes following administration, and more preferably for at least 150 minutes after  
20 administration. Preferably, the trehalose is administered no more than one hour before the start of exercise, and more preferably no more than 10 minutes before the exercise, and most preferably during the exercise. In particularly preferred methods, the administration during the exercise may be in addition to administration before the start of exercise.

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Preferably, the blood glucose level is maintained for at least one hour following the physical exercise, and more preferably for at least 90 minutes following the physical exercise.

30 Specific examples of the present invention will now be described further in the following procedures and examples, with reference to the accompanying drawings, in which:-

Figure 1 shows a graph of blood plasma glucose concentration against time during a cycle ride to exhaustion at 70%  $\text{VO}_2\text{max}$ . Data are shown for subjects given a placebo (filled circles), a 5 wt.% glucose sports drink (open circles) and a 10 wt.% trehalose sports drink (open squares).

5

Figure 2 shows graphs of plasma insulin concentration against time measured for the subjects in the experiment of Figure 1.

### Procedure 1

10 The effects of a trehalose solution on metabolic responses, perception of effort, and endurance performance during exercise to exhaustion at a constant exercise intensity were assessed as follows.

Nine healthy male human volunteers, aged  $21 \pm 1$  years (mean  $\pm$  S.E.M.),  
15 body mass  $81.8 \pm 2.0$  kg, height  $1.79 \pm 0.02$  m, body mass index (BMI)  $25.4 \pm 0.5$   $\text{kg/m}^2$  volunteered as subjects for the experiment and gave written informed consent. All subjects were recreationally active and familiar with exercise sessions lasting 1-3 hours. None of the subjects had suffered an illness in the preceding 3 weeks. None of the subjects had recently modified their dietary  
20 energy intake and none had undergone marked weight changes in the previous 3 months. Subjects were required to abstain from alcohol intake in the 24 hours preceding each experimental trial. All subjects were given a test drink containing 5 g trehalose prior to commencing the main study. None of the subjects reported any gastrointestinal discomfort following the test drink.

25

The aerobic fitness of the subjects was quantified by measurement of their maximal oxygen uptake ( $\text{VO}_2\text{max}$ ). Maximal oxygen uptake was determined using a continuous incremental protocol on an electrically braked cycle ergometer (Lode Excalibur (Registered Trade Mark), Holland). Following a 3-minute warm-up at  
30 120W, subjects began cycling at an initial work rate of 150W with increments of 30W every 2 minutes until fatigue. During the second minute of each work rate an expired gas sample was collected into a Douglas bag. A paramagnetic oxygen analyser (Servomex 1420B (Registered Trade Mark), Crowborough, UK) and an

infrared carbon dioxide analyser (Servomex 1415B) were used along with a dry gas meter (Harvard Apparatus Ltd, Edenbridge, UK) for determination of minute ventilation,  $\dot{V}O_2$  and  $\dot{V}CO_2$ . The BASES criteria for attainment of  $\dot{V}O_{2max}$  were adopted. From the  $\dot{V}O_2$ -work rate relationship, the work rate equivalent to 70%  $\dot{V}O_{2max}$  was interpolated.

Subjects performed three bouts of exercise on separate occasions at least one week apart. Following an overnight fast, subjects cycled on cycle ergometer at a work rate equivalent to 70%  $\dot{V}O_{2max}$  until exhaustion. On each of these occasions the subjects were randomly assigned to one of three experimental treatments: glucose (5% w/v), trehalose (10% w/v) or placebo solutions. Each solution was flavoured with sugar-free lemon cordial and contained 20 mmol/l trisodium citrate. The osmolality of the drinks was measured using a freezing point osmometer (Advanced Instruments) and was 110, 361, and 386 mOsm/kg for the PLA, GLU, and T10 drinks, respectively (note that 80 mOsm/kg of each drink was attributable to the added trisodium citrate). The treatments were blinded to the subjects.

Subjects reported to the laboratory in the morning following an overnight fast and nude body weight was recorded. Subjects were instructed to keep their daily exercise to a minimum during the 72 hours preceding each exercise test and to standardise their diet for the 24 hours prior to each test. A 4 cm, 21 g Venflon (Registered Trade Mark) cannula was inserted into an antecubital vein and an initial resting blood sample was obtained. Immediately after this the subject consumed 5 ml per kg body mass of the prescribed drink and then began cycling at 70%  $\dot{V}O_{2max}$  until volitional fatigue. Further blood samples were obtained at 15-minute intervals during exercise and at test cessation. Following each blood sample subjects ingested 2 ml per kg body mass of their prescribed solution. Heart rate was monitored at 15-minute intervals using a radiotelemetric device (Polar Electro, Kempele, Finland) and samples of expired gas were collected into Douglas bags after 35, 70 and 105 minutes of exercise for determination of  $\dot{V}O_2$  and respiratory exchange ratio. Whole body rates of carbohydrate oxidation were estimated from the gas exchange measurements. Ratings of perceived exertion

(Borg, 1982) were made at 15-minute intervals. Immediately after the post-exercise blood sample has been obtained, subjects towelled dry and nude body weight was measured. Further blood samples were obtained at 1, 2.5 and 4 hours post-exercise, with the subject in a seated position. The subjects consumed an additional 5 ml per kg body mass of the prescribed drinks immediately following the blood samples taken at 1 and 2.5 hours post-exercise. Room conditions were  $19.3 \pm 0.3$  °C and  $58 \pm 2\%$  relative humidity.

Blood was placed into EDTA tubes (4.5 ml) and lithium heparin tubes (7 ml). An aliquot from the EDTA tube was used to determine haemoglobin concentration and haematocrit so that plasma volume changes can be estimated according to Dill and Costill (1974). The remainder was used for analysis of differential white blood cell counts (not reported here). Blood from the heparinised tube was centrifuged at 1500 g for 10 minutes at 4°C to obtain plasma. The latter was stored at -70°C prior to analysis for glucose and lactate (Sigma Chemicals kits), insulin and cortisol (by radioimmunoassay using ICN Biomedicals antibody coated tube kits), and total protein (Biuret method; Sigma Chemicals). The coefficient of variation for the assays was  $\pm 2.4\%$  for glucose,  $\pm 7.3\%$  for lactate,  $\pm 3.4\%$  for protein  $\pm 3.5\%$  for insulin and  $\pm 2.4\%$  for cortisol.

20

Differences with time and treatment were assessed using a repeated measures ANOVA with Tukey post hoc tests where appropriate. The accepted level of significance was  $P < 0.05$ . Friedman's non-parametric test was also used where appropriate (e.g. for endurance times and body mass changes). All data in the text, Tables and Figures are reported as mean  $\pm$  standard error of the mean (S.E.M.) for eight subjects from whom we obtained the full complement of blood samples.

25

The mean  $\text{VO}_2\text{max}$  of the subjects was  $53.1 \pm 1.9$  ml/kg/min and the mean work rate equivalent to 70%  $\text{VO}_2\text{max}$  used in the exercise trials was  $198 \pm 12$  W. Oxygen uptakes averaged for the 35 and 70-minute time points during exercise were  $78.5 \pm 4.1\%$ ,  $76.6 \pm 3.4\%$  and  $72.8 \pm 2.6\%$   $\text{VO}_2\text{max}$  for the PLA, GLU and T10 trials, respectively (no significant difference between trials,  $P > 0.05$ ). The

30

mean total fluid intakes (up to the end of exercise) were  $1113 \pm 86$  ml,  $1257 \pm 84$  ml and  $1163 \pm 102$  ml for the placebo (PLA) 5% w/v glucose (GLU) and 10% w/v trehalose (T10) drinks, respectively. The mean total sugar intakes (up to the end of exercise) were  $62.8 \pm 4.2$  g and  $116.3 \pm 10.2$  g for the glucose and trehalose treatments, respectively.

Time to fatigue was  $77 \pm 8$ ,  $98 \pm 8$  and  $86 \pm 10$  minutes on the PLA, GLU and T10 trials, respectively. Performance on the GLU trial was significantly longer than on the PLA trial ( $P < 0.05$ ). Performance on the T10 trial was not significantly different from that on the GLU or PLA trial. Six of the nine subjects cycled for longer on T10 than on PLA, but only two of the subjects cycled for longer on T10 than on GLU. Interestingly, these two subjects had the longest endurance times among this subject group.

From the oxygen uptake and RER data, it was calculated that the rate of carbohydrate oxidation during exercise was similar on all treatments.

Heart rate was similar on all three trials and averaged  $165 \pm 4$  beats/min after 30 minutes of cycling and  $172 \pm 5$  beats/min at exhaustion. Perceived exertion was not significantly affected by glucose or trehalose ingestion compared with placebo.

Resting plasma lactate concentration was  $0.8 \pm 0.1$  mmol/l and at exhaustion had increased to  $3.5 \pm 0.7$ ,  $3.0 \pm 0.5$  and  $3.1 \pm 0.4$  mmol/l on the PLA, GLU and T10 trials, respectively. There were no significant differences in the plasma lactate response to exercise between trials.

The mean resting plasma glucose concentration before consumption of the drinks was 5.4 mmol/l. The change in plasma glucose concentration during exercise on the different trials is shown in Figure 1. There was a significant Time\*Trial interaction ( $F_{8,64} = 3.60$ ;  $P < 0.05$ ) for the plasma glucose responses. On the PLA treatment the plasma glucose concentration fell significantly during exercise and at exhaustion was 4.6 mmol/l. On the GLU and T10 trials, plasma

glucose concentration was maintained at or slightly above pre-exercise levels throughout exercise. At 1 hour and 2.5 hours post-exercise, the plasma glucose concentration on the T10 trial was significantly higher than on GLU or PLA (both  $P < 0.05$ ). This demonstrates the sustained nature of glucose release following  
5 ingestion of the trehalose.

Changes in plasma volume were small but there was a significant fall in plasma volume during the first 15 minutes of exercise on all trials which was gradually restored during the remainder of the exercise bouts. At the end of  
10 exercise, changes in plasma volume were  $-6.5 \pm 1.9\%$ ,  $-6.2 \pm 1.8\%$ , and  $-7.8 \pm 1.4\%$  for the PLA, GLU, and T10 trials, respectively. Body mass changed by a similar amount on all three trials, falling on average by only 0.2 kg. Taking into account the volume of fluid consumed during the trials, sweat losses amounted to  $1.4 \pm 0.2$  litres during exercise.

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There was a main effect of time on the plasma protein concentration ( $F_{4,32} = 3.57$ ;  $P < 0.02$ ) which increased on average by 8% during the exercise trials but there were no significant differences between the treatments.

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The mean resting plasma insulin concentration before consumption of the drinks was 14 mU/l. The change in plasma insulin concentration during the three exercise trials is shown in Figure 2. There was a significant Time\*Trial interaction ( $F_{4,32} = 5.27$ ;  $P < 0.05$ ) for the plasma insulin responses. On the PLA treatment the plasma insulin concentration fell significantly during exercise. Following GLU and  
25 T10 ingestion, plasma insulin concentration was maintained at pre-exercise levels throughout exercise. At 1 hour, 2.5 hours and 4 hours post-exercise the plasma insulin concentration was significantly higher on the T10 trial compared with both the GLU trial ( $P < 0.05$ ) and the PLA trial ( $P < 0.01$ ).

30

At exhaustion, plasma cortisol concentration had increased significantly on all trials compared with pre-exercise, although there were no significant differences between trials.

Example 1

A sports drink for use in accordance with the present invention is prepared from the following ingredients:

5	Trehalose dihydrate	83.3 g
	Acesulfame K	0.03 g
	Aspartame	0.03 g
	Lemon juice concentrate	25 ml

10 The ingredients are dissolved in 0.5 litres of water at 25°C, and when fully dissolved the liquid is made up to 1.0 litres with water. The solution is allowed to stand for 30 minutes before use.

The sports drink will normally be consumed in an amount of 100 to 500 ml during or shortly before vigorous exercise.

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The above embodiments have been described by way of example only. Many other embodiments of the present invention as defined in the accompanying claims will be apparent to the skilled reader.

## CLAIMS

1. Use of trehalose for the preparation of a nutritional composition for oral administration to a subject during and/or shortly before prolonged physical exercise to maintain the blood glucose level of the subject for a sustained period after said exercise.
2. Use of trehalose for the preparation of a nutritional composition for oral administration to a subject during and/or shortly before prolonged physical exercise to reduce physical and mental impairment of the subject following said exercise.
3. Use of trehalose for the preparation of a nutritional composition for oral administration to a subject during and/or shortly before prolonged physical exercise to promote post-exercise recovery.
4. Use according to any preceding claim, wherein the nutritional composition is selected from the group consisting of chocolate confectionery, sugar confectionery, biscuits, fondants, jellies, jams, sauces, puddings, syrups, soft drinks, sweet or savoury snack foods, cakes and other baked goods, ice cream, and combinations thereof.
5. Use according to claim 4, wherein the nutritional composition is a soft drink.
6. Use according to claim 5, wherein the step of preparation comprises diluting concentrate with water.
7. Use according to claim 5 or 6, wherein the soft drink has an osmolarity of 400 mOsm or less.
8. Use according to claim 5, 6 or 7, wherein the soft drink also comprises at least one salt in an amount sufficient to enhance uptake of the water through the intestinal tract.

9. Use according to claim 6 wherein the salt is selected from the group consisting of salts of sodium, potassium, magnesium and calcium.

5 10. Use according to any preceding claim, wherein the nutritional composition also comprises one or more nutritional supplements selected from the group consisting of vitamins, minerals, amino acid residues and mixtures thereof.

11. Use according to claim 10, wherein the nutritional composition comprises a  
10 mineral supplement selected from the group consisting of iron, zinc, chromium, calcium, copper, magnesium and mixtures thereof.

12. Use according to any preceding claim, wherein the nutritional composition also comprises a stimulant.

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13. Use according to claim 12, wherein the stimulant is selected from the group consisting of caffeine and taurine and mixtures thereof.

14. Use according to any preceding claim, wherein the step of oral  
20 administration comprises administration of at least 0.1 g of trehalose per kg body weight of the person, preferably at least 0.3g/kg and more preferably at least 0.5 g/kg.

15. Use according to any preceding claim, wherein the step of oral  
25 administration comprises administration of more than 12 g of trehalose, preferably more than 20 g of trehalose.

16. Use according to any preceding claim, wherein the composition comprises at least 10% w/w of trehalose, preferably at least 20% w/w of trehalose, more  
30 preferably at least 30% w/w trehalose, and most preferably at least 40% or 50% by weight of trehalose, based on the dry weight of the composition.

17. Use according to any preceding claim, wherein the physical exercise is prolonged for at least 20 minutes, more preferably 30 minutes or more.

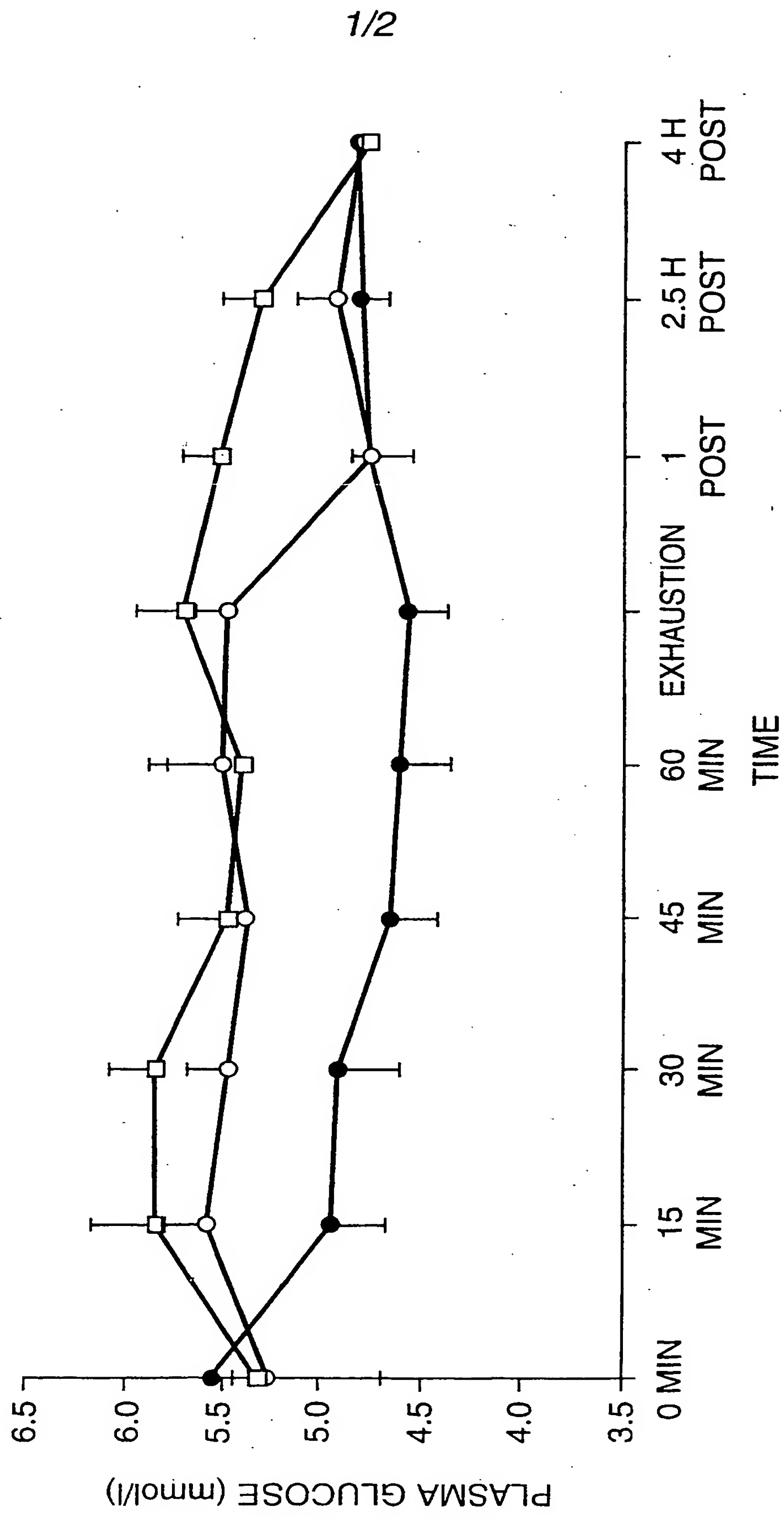
18. Use according to any preceding claim, wherein the blood glucose level is maintained at a level at least 0.25 mmol/l above the level for a carbohydrate-free placebo of equal liquid volume.

19. Use according to any preceding claim, wherein the blood glucose level is maintained for at least 2 hours following administration.

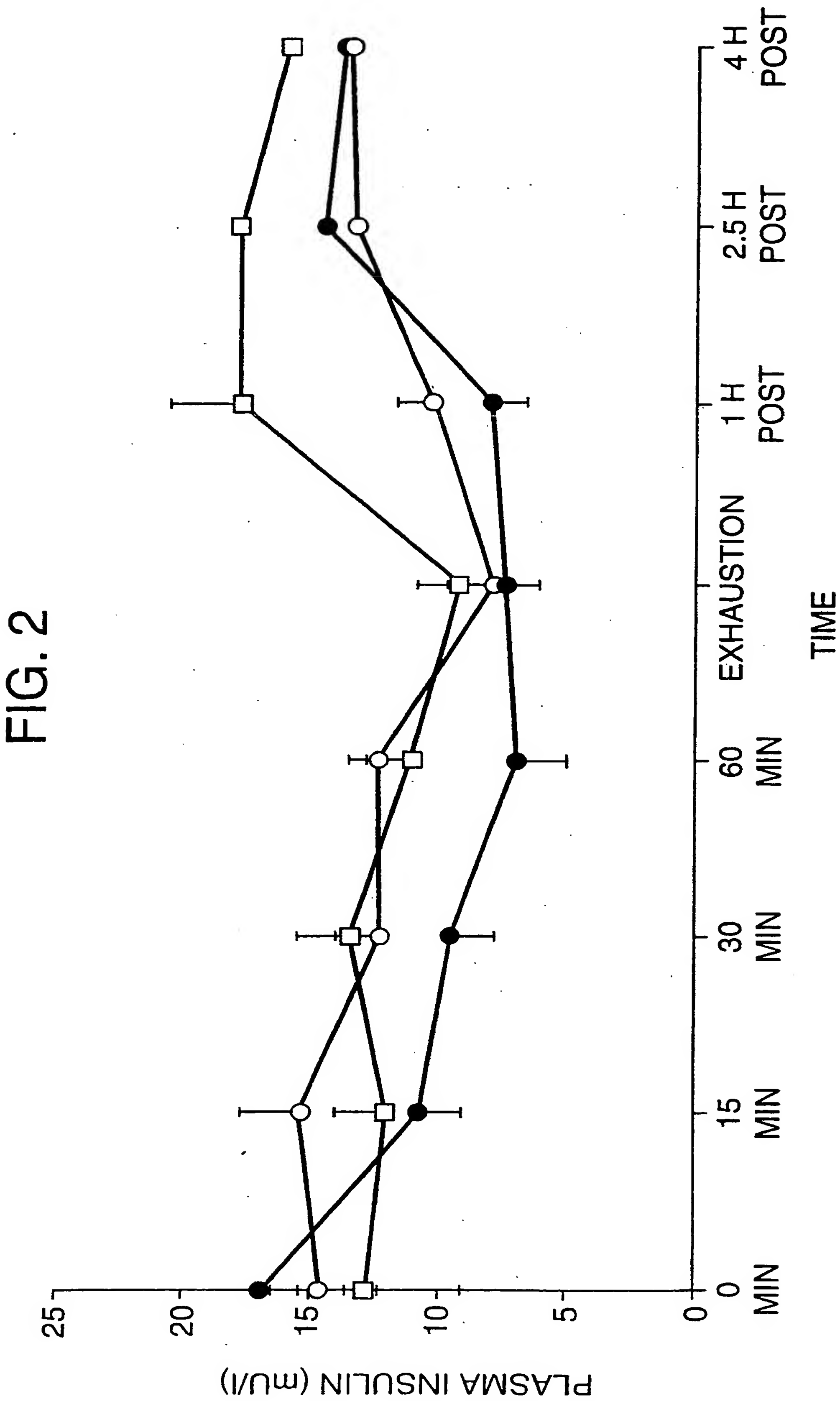
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20. Use according to any preceding claim, wherein the blood glucose level is maintained for at least one hour following the said physical exercise.

FIG. 1



2/2



# INTERNATIONAL SEARCH REPORT

In. ational Application No  
PCT/GB 00/04608

**A. CLASSIFICATION OF SUBJECT MATTER**  
IPC 7 A23L1/30 A23L2/38 A23L2/52 A23L1/09

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
IPC 7 A23L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, FSTA

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 96 08979 A (QUADRANT HOLDINGS CAMBRIDGE ;KAMPINGA JAPP (GB); COLACO CAMILO ANT) 28 March 1996 (1996-03-28) cited in the application claims 1,5-9,12-17,21-25; examples 1-5 page 1, paragraph 1 page 3, line 3 page 5, paragraph 3 -page 7, paragraphs 1,3,4 page 9, paragraph 3 -page 10, paragraph 1 ---	1-12,16, 17
A		13-15, 18-20
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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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Date of the actual completion of the international search

19 March 2001

Date of mailing of the international search report

30/03/2001

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# INTERNATIONAL SEARCH REPORT

Int. Application No  
PCT/GB 00/04608

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X  A	<p>EP 0 619 951 A (HAYASHIBARA BIOCHEM LAB) 19 October 1994 (1994-10-19) cited in the application claims 1,4,5,10,11; figures 1-6; examples 1-12 page 2, line 27-43 page 3, line 5-14,43-53 page 5, line 55 -page 7, line 4 ---</p>	<p>1-6, 10-12, 14-20 7-9,13</p>
X  A	<p>EP 0 983 726 A (RIKEN ;MEIJI MILK PROD CO LTD (JP)) 8 March 2000 (2000-03-08)  claims 1,3; figure 2; example 1  page 2, line 3-12,33-48 page 3, line 21,22 page 4, line 19-29 page 5, line 55 -page 6, line 7 ---</p>	<p>1-6,10, 12-14, 16-18,20 7-9,11, 15,19</p>
X  A	<p>EP 0 532 807 A (HAYASHIBARA BIOCHEM LAB) 24 March 1993 (1993-03-24)  claims 1-3,5-8,10 page 2, line 56 -page 3, line 12 page 4, line 28-51  page 7, line 25 -page 8, line 20 page 8, line 45 -page 9, line 24,43-49 ---</p>	<p>1-6, 8-10, 14-17   7,11-13, 18-20</p>
X  A	<p>EP 0 834 516 A (HAYASHIBARA BIOCHEM LAB) 8 April 1998 (1998-04-08)  page 17, line 49 -page 18, line 23 ---</p> <p>DE 40 22 058 A (OETKER NAHRUNGSMITTEL) 16 January 1992 (1992-01-16) claims 4,7; example 2 column 3, line 62-68 ---</p>	<p>1-6, 8-10,12, 13,17</p> <p>1-20</p>
X  A	<p>DATABASE WPI Section Ch, Week 199737 Derwent Publications Ltd., London, GB; Class D13, AN 1997-396989 XP002163278 &amp; JP 09 173017 A (LOTTE CO LTD), 8 July 1997 (1997-07-08) cited in the application abstract ---</p> <p>PATENT ABSTRACTS OF JAPAN vol. 1999, no. 09, 30 July 1999 (1999-07-30) &amp; JP 11 089547 A (MORINAGA &amp; CO LTD), 6 April 1999 (1999-04-06) abstract -----</p>	<p>1-4,17</p> <p>1-20</p>

# INTERNATIONAL SEARCH REPORT

Information on patent family members

In. tional Application No

PCT/GB 00/04608

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9608979 A	28-03-1996	AU 3570495 A CZ 9700886 A EP 0782398 A JP 10508744 T	09-04-1996 17-09-1997 09-07-1997 02-09-1998
EP 0619951 A	19-10-1994	AU 681109 B AU 5782394 A CA 2119070 A CN 1101832 A IL 108965 A JP 6319486 A US 5576303 A	21-08-1997 22-09-1994 17-09-1994 26-04-1995 15-07-1998 22-11-1994 19-11-1996
EP 0983726 A	08-03-2000	JP 2000072669 A	07-03-2000
EP 0532807 A	24-03-1993	JP 5076308 A JP 5078234 A CA 2055257 A US 5604211 A	30-03-1993 30-03-1993 21-03-1993 18-02-1997
EP 0834516 A	08-04-1998	JP 10165118 A US 5916881 A	23-06-1998 29-06-1999
DE 4022058 A	16-01-1992	BR 9102927 A CH 681501 A DK 20391 A FR 2664472 A IT T0910538 A NL 9100319 A	28-04-1992 15-04-1993 12-01-1992 17-01-1992 13-01-1992 03-02-1992
JP 9173017 A	08-07-1997	NONE	
JP 11089547 A	06-04-1999	NONE	

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